The Robert Jones and Agnes Hunt Orthopaedic Hospital

NHS Foundation Trust

Adjuvant Therapies

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The Oswestry BONE CANCER CENTRE

The Plan

- **Overview**

Therapies Available
- **Radiation therapy**
- **Chemotherapy**
- **Targeted therapies**
- **Denosumab**

- **Bone and soft tissue sarcoma**
- **Metastatic disease**


WARNING
IONIZING
RADIATION
CAUTION
CHEMOTHERAPY DRUG
OBSERVE SAFETY
PRECAUTIONS FOR
Surgery

Terminology

- Adjuvant
  - ‘in addition to’ eg post-op
- Neo-adjuvant
  - ’before primary treatment’ eg pre-op

FRCS question:	How is osteosarcoma treated in the UK?
FRCS answer:	Via a MDT approach, with neoadjuvant chemotherapy, then surgery followed by further chemotherapy

Mode of action for chemotherapy and radiation therapy

DNA damage

Normal cells are also damaged but have the ability to replicate. Cancer cells **do not**

Treatments are fractionated or in cycles to kill cancer cells going through each stage of the cell cycle, and give normal cells the opportunity to recover

Ideal time to ‘kill is when undergoing cell division

Radiation Therapy

- External beam radiotherapy
  - Photons
  - Particle beam (protons or carbon)
- Brachytherapy (& unsealed sources such as iodine)
  - Inside or next to the tumour
  - Gynae/prostate
- Stereotactic
  - Highly accurate low dose overlapping beam
  - CNS tumours

Indications for Radiotherapy in MSK Malignancy

- Soft tissue sarcoma
  - Central to management
    - Neoadjuvant or adjuvant
    - High-dose
- Bone sarcoma
  - OS - relatively radioresistant
  - ChS – radioresistant
  - EwS - some uses
- Metastatic
  - Palliative
    - Symptom relief for bone mets

Sarcoma radiotherapy

Hoefkens *et al. Radiation Oncology* (2016) 11:136
DOI 10.1186/s13014-016-0668-9

Radiation Oncology

REVIEW Open Access

Soft tissue sarcoma of the extremities: pending questions on surgery and radiotherapy

Fien Hoefkens[1], Charlotte Dehandschutter[1], Johan Somville[1,2], Paul Meijnders[1,3] and Dirk Van Gestel[3,4*]

Gerrand *et al. Clin Sarcoma Res (2016) 6:7*
DOI 10.1186/s13569-016-0047-1

Clinical Sarcoma Research

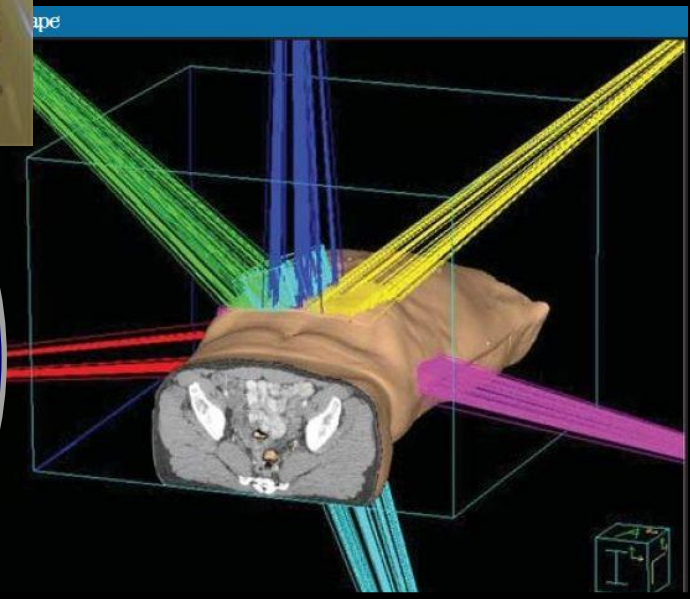
REVIEW Open Access

UK guidelines for the management of bone sarcomas

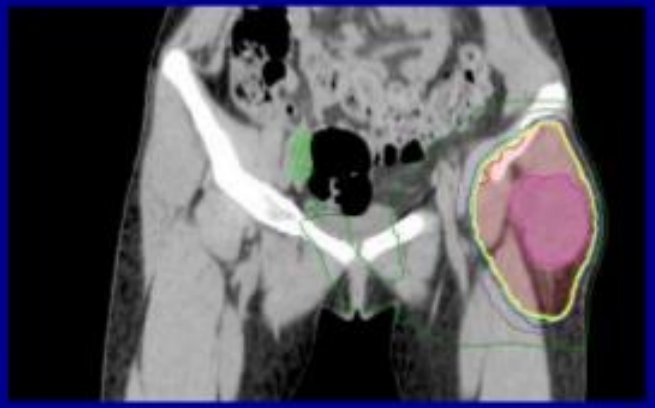
Craig Gerrand[1*], Nick Athanasou[2], Bernadette Brennan[3], Robert Grimer[4], Ian Judson[5], Bruce Morland[6], David Peake[7], Beatrice Seddon[8], Jeremy Whelan[8] and On behalf of the British Sarcoma Group

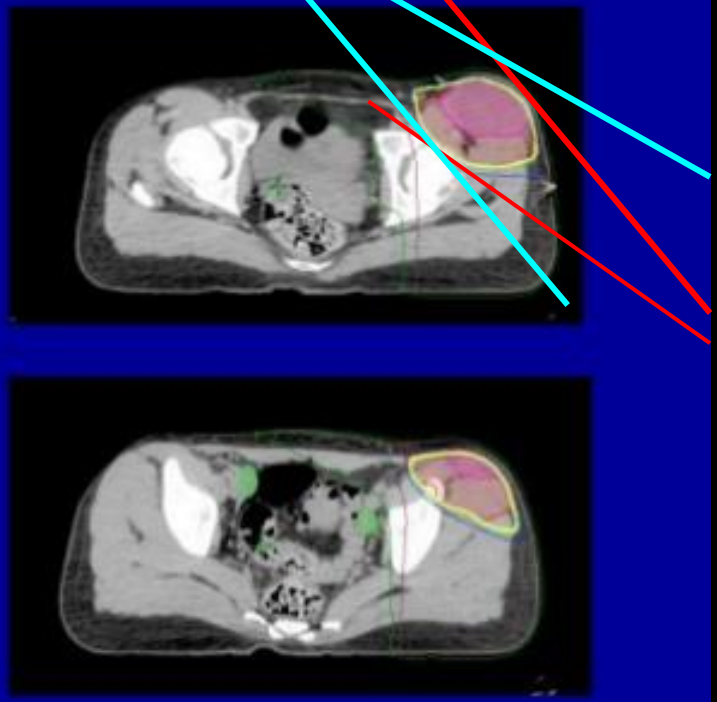
External beam radiotherapy

- Photons = high energy xrays
- Releases energy in and through the tissue
- Side effects related to the tissue it is exposed to
- High precision with new techniques - IMRT



Radiation Graphic Plan





Pink: tumor; Green: ovaries

Dose Lines:

100%	Yellow
90%	Blue
40%	Brown
6%	Green

Proton beam radiotherapy

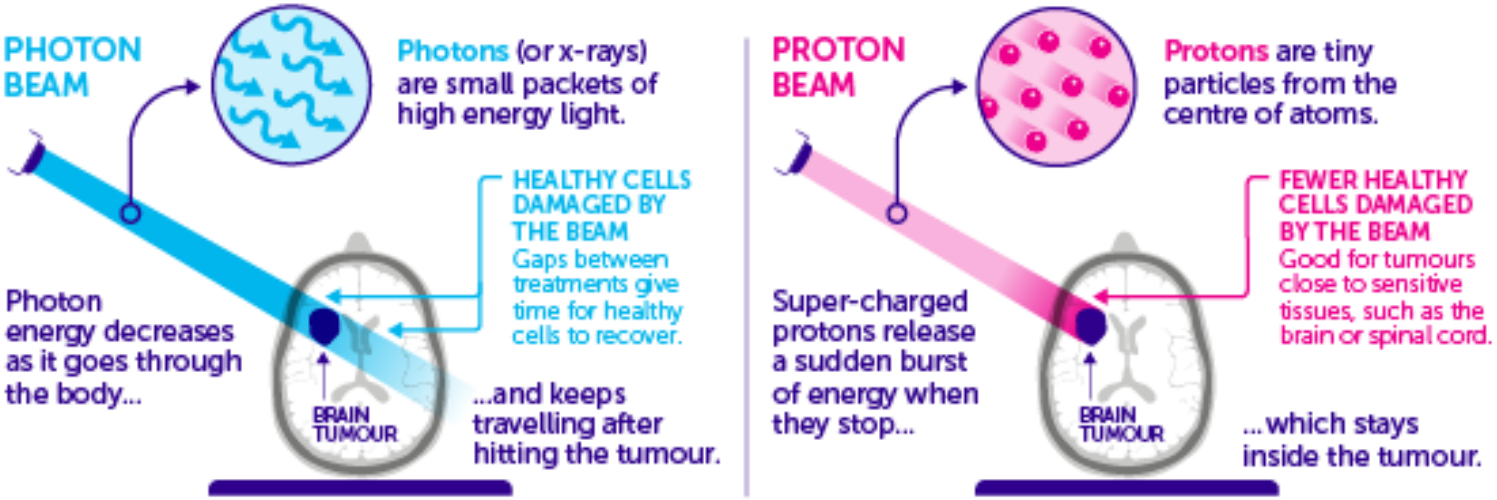
- Protons = heavy subatomic particles
- Releases energy in tissue when decelerated rapidly
- Side effects related to the tissue it is exposed to, especially skin

The 250 Million Pound Cancer Cure, Horizon. BBC Two

https://www.bbc.co.uk/programmes/m00072kd

PHOTON AND PROTON RADIOTHERAPY WHAT'S THE DIFFERENCE?

Radiotherapy targets tumours with a beam of energy which damages DNA and kills cancer cells.



LET'S BEAT CANCER SOONER
cruk.org

CANCER RESEARCH UK

Pre or Post-op Radiotherapy (STS)?

PRE

- Smaller volume
  - Target the tumour not surgical bed
- Radiotherapy planning easier
- Reduction of late complications
  - Fibrosis, stiffness, oedema

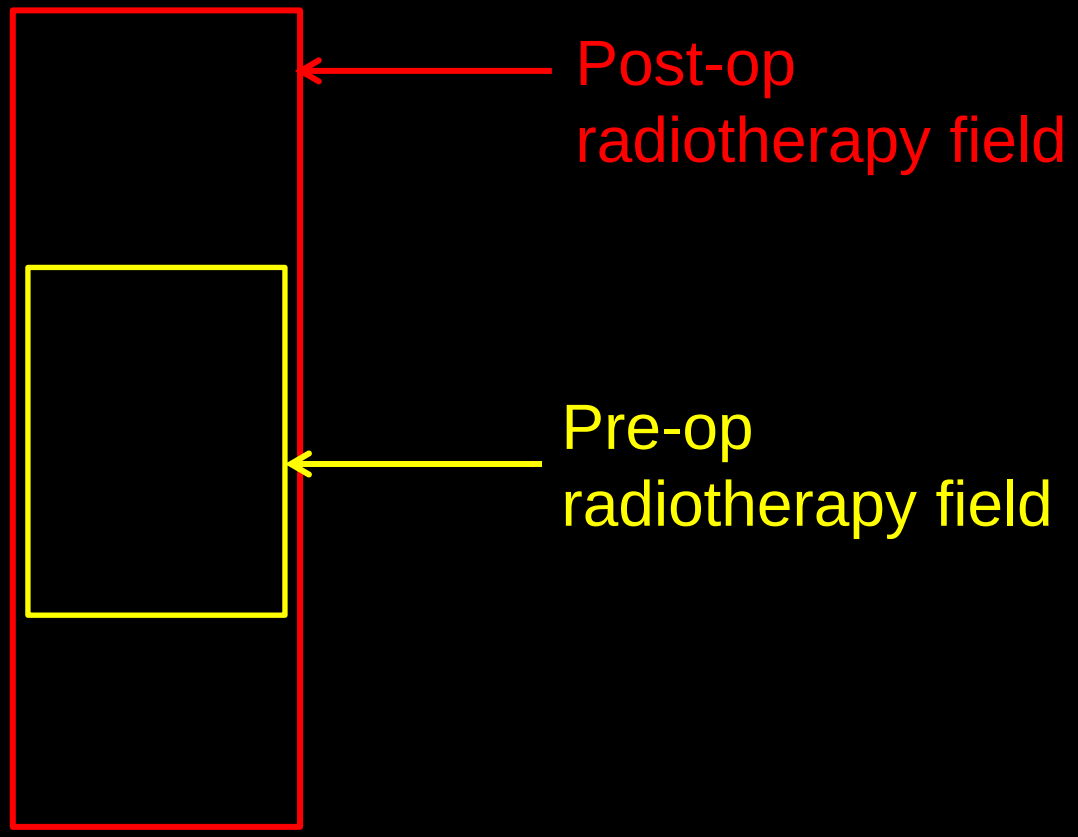
POST

- Better staging
- Tumour response not a factor
- Surgery dissection easier

Pre-op = Is the standard

BUT

If its growing, or expected surgical difficulty post radiation – for surgery then radiotherapy


Post-op
radiotherapy field
Pre-op
radiotherapy field

Chemotherapy

- Standard treatment for
  - OS
  - EwS

** neoadjuvant and adjuvant**

OS: MAP regime
Methetraxate
Doxurubicin
Cisplatin

EwS: VIDE regime
Vincristine
Ifosfamide
Doxorubicin
Etoposide

- Palliative option
  - STS

Ewings Management Plan

Chemo

Chemo

Chemo

Chemo

Chemo

Chemo

12 months timeline

Surgery

Chemo

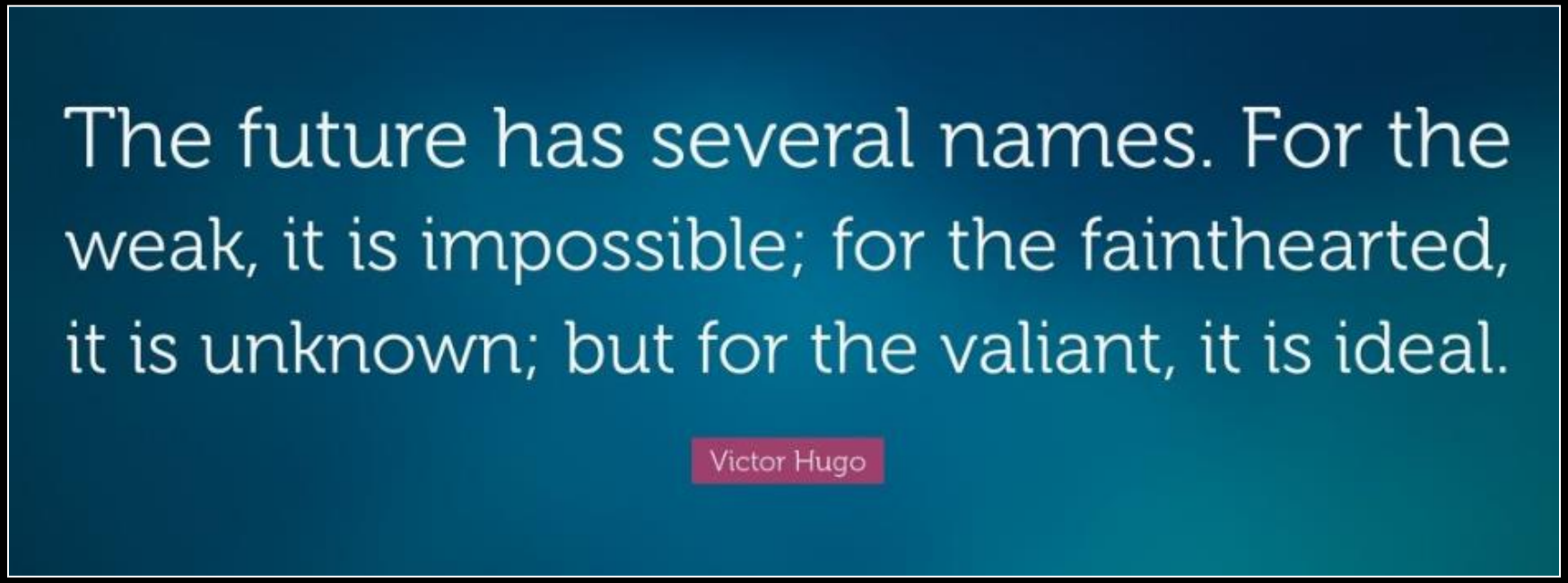
Chemo

Chemo

Or post op RT

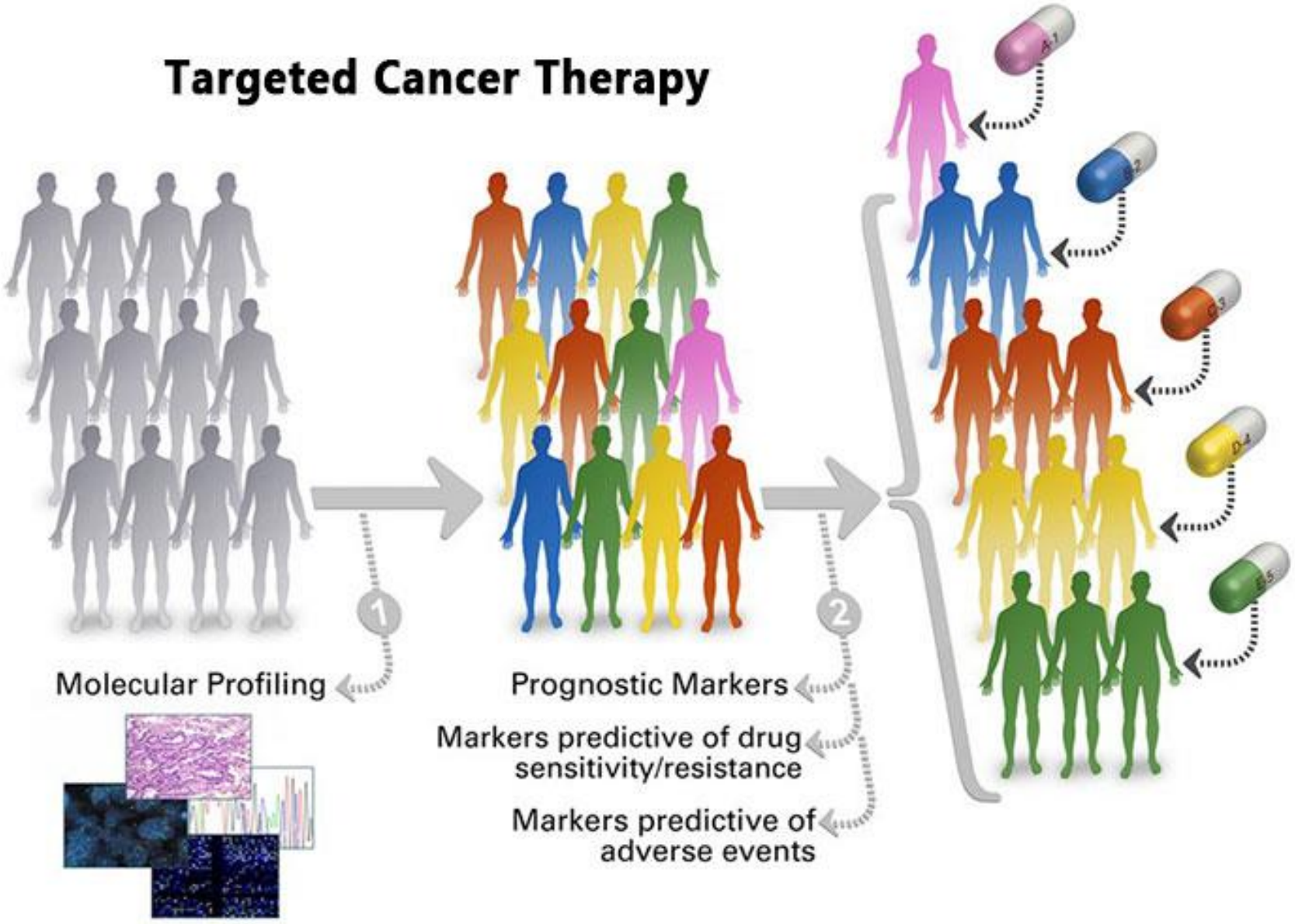
Pre-op RT

Targeted therapies



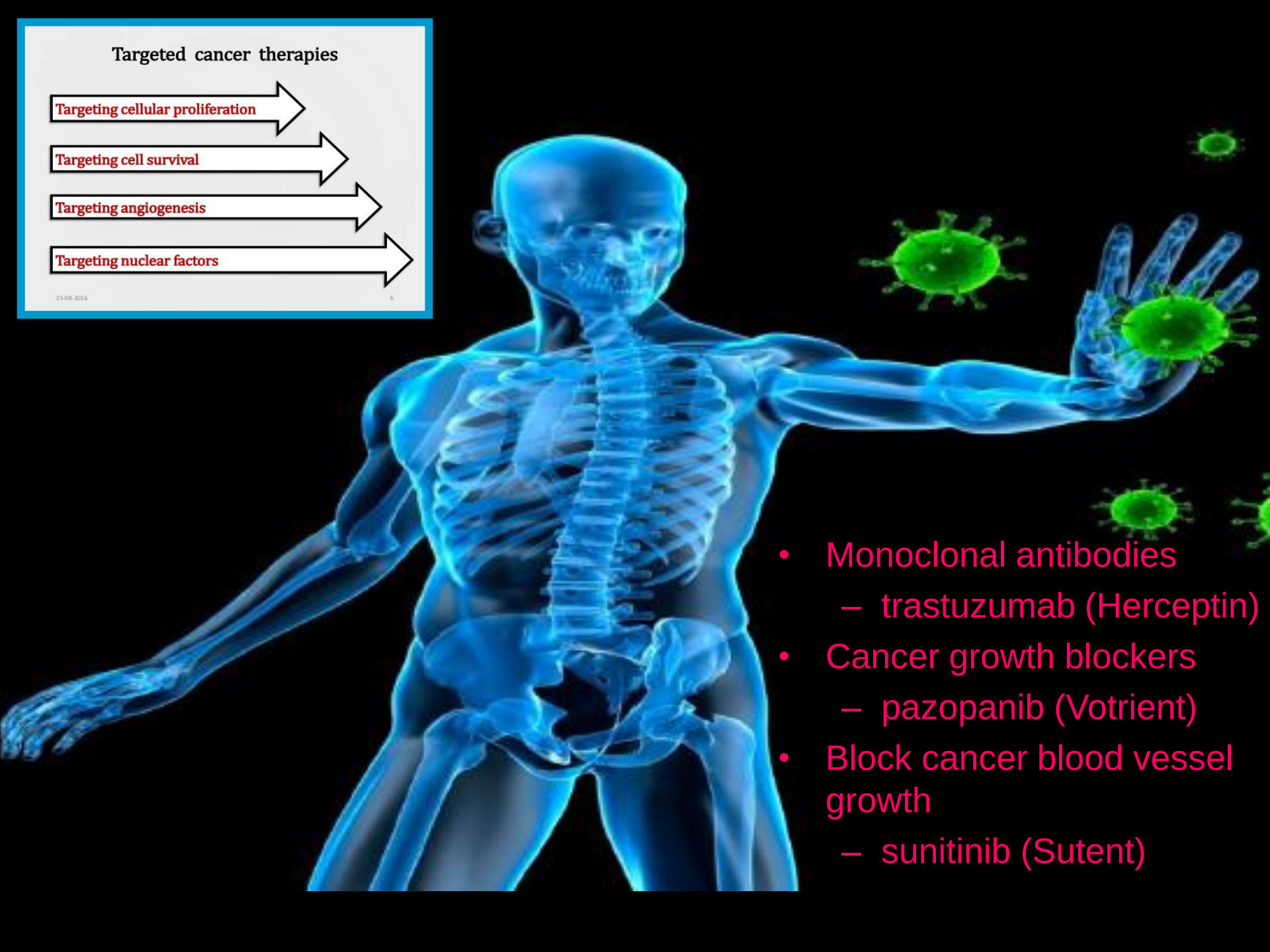
Targeted Therapies Pick Out Cancer Cells

Targeted Cancer Therapy

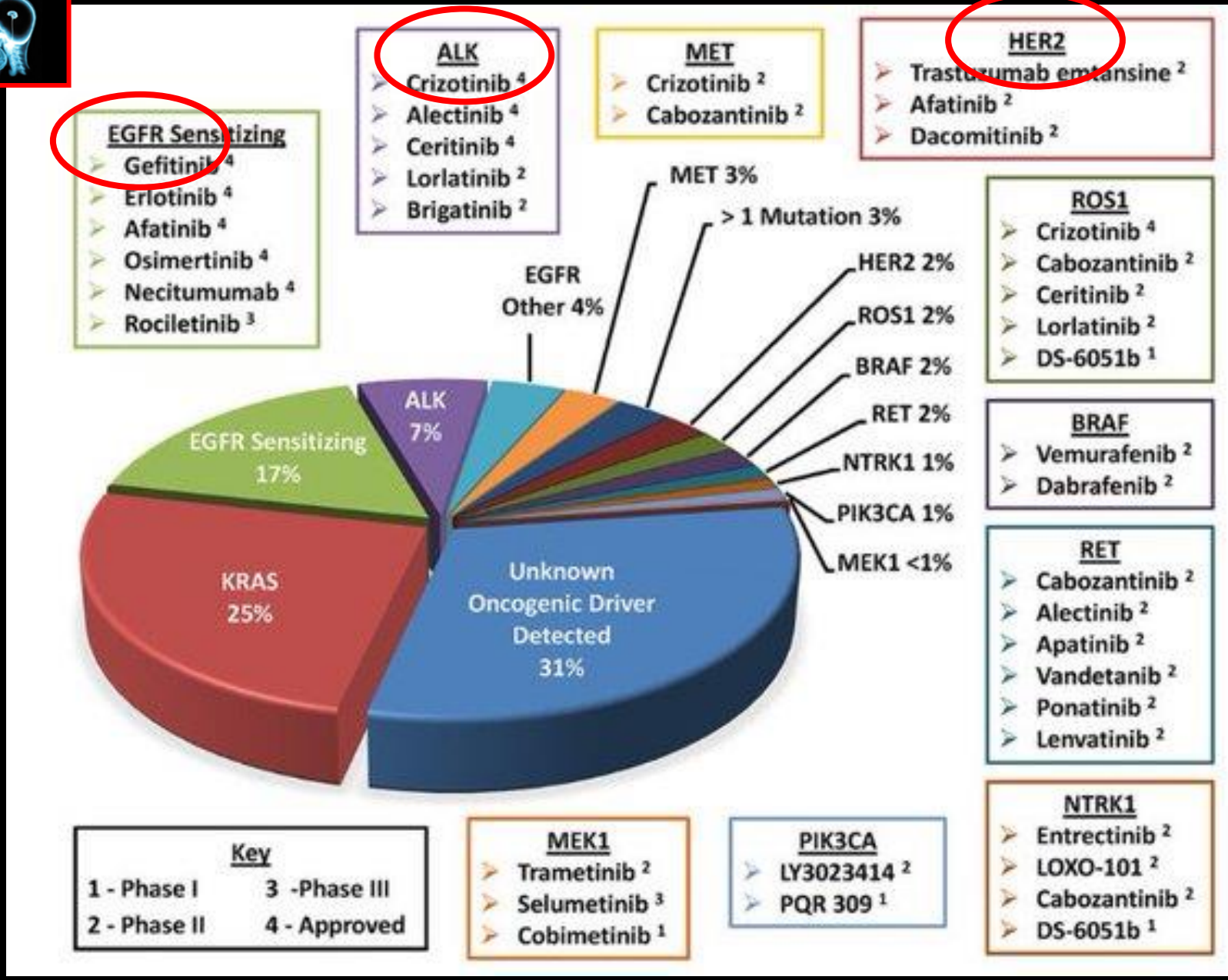


Targeted cancer therapies

- Targeting cellular proliferation
- Targeting cell survival
- Targeting angiogenesis
- Targeting nuclear factors

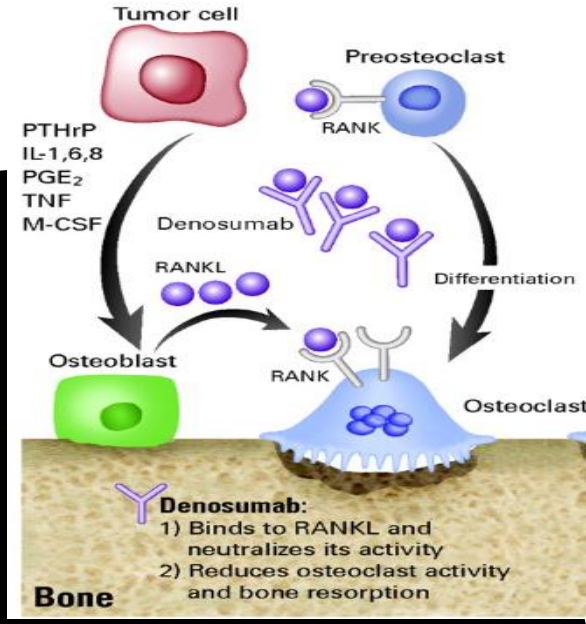


- Monoclonal antibodies
  - trastuzumab (Herceptin)
- Cancer growth blockers
  - pazopanib (Votrient)
- Block cancer blood vessel growth
  - sunitinib (Sutent)

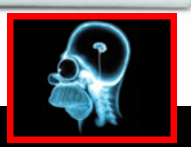

ALK
Crizotinib 4
Alectinib 4
Ceritinib 4
Lorlatinib 2
Brigatinib 2
MET
Crizotinib 2
Cabozantinib 2
HER2
Trastuzumab emtansine 2
Afatinib 2
Dacomitinib 2
EGFR Sensitizing
Gefitinib 4
Erlotinib 4
Afatinib 4
Osimertinib 4
Necitumumab 4
Rociletinib 3
MET 3%
> 1 Mutation 3%
HER2 2%
ROS1 2%
BRAF 2%
RET 2%
NTRK1 1%
PIK3CA 1%
MEK1 <1%
EGFR Other 4%
ALK 7%
EGFR Sensitizing 17%
KRAS 25%
Unknown Oncogenic Driver Detected 31%
ROS1
Crizotinib 4
Cabozantinib 2
Ceritinib 2
Lorlatinib 2
DS-6051b 1
BRAF
Vemurafenib 2
Dabrafenib 2
RET
Cabozantinib 2
Alectinib 2
Apatinib 2
Vandetanib 2
Ponatinib 2
Lenvatinib 2
NTRK1
Entrectinib 2
LOXO-101 2
Cabozantinib 2
DS-6051b 1
Key
1 - Phase I
2 - Phase II
3 -Phase III
4 - Approved
MEK1
Trametinib 2
Selumetinib 3
Cobimetinib 1
PIK3CA
LY3023414 2
PQR 309 1

Denosumab

- Monoclonal antibody
  - RANKL inhibitor
- Mode of action
  - Osteoclastic inhibition
- Indications
  - bone mets
  - GCT
  - osteoporosis



- Risks
  - Osteonecrosis
  - Hypercalcaemia
  - Fertility/teratogenic
  - Atypical fracture
- Administration
  - Usually monthly
  - Under supervision oncology
  - Teeth check



The Future

- Side effect profile
- Prognosis
- Long term impact

Questions

Learning Point Summary

- Surgery is the primary intervention in sarcoma management
- Chemotherapy & radiotherapy act by damaging cellular DNA. Normal cells recover
- Targeted therapies interfere with molecular processes and can be personalised
- Genetic mapping is changing cancer management and prognosis
- Denosumab is a new-ish but highly used drug in MSK oncology. RANKL mediated.